Complete if Known

10/611,363

Substitute for form 1449A/PTO (Modified)

## ÍNFORMATION DISCLOSURE STATEMENT BY APPLICANT

Filing Date July 1, 2003 DESJARLAIS, John R. First Named Inventor 1647 Art Unit

(use as many sheets as necessary)

Examiner Name To Be Assigned A-71486-2 1 6 Attorney Docket Number Sheet

Application Number

				U.S. PATENT D	OCUMENTS	
Iniuais		Cite No.1	U.S. Patent Document Number-Kind Code <sup>2</sup> ( <i>if known</i> )	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	)	A1	5,843,678	12-01-1998	Boyle	
		A2	6,017,729	01-25-2000	Anderson et al.	
	+	A3 *	6,188,965 B1	02-13-2001	Mayo et al.	
		A4 *	6,269,312 B1	07-13-2001	Mayo et al.	
		A5	6,316,408 B1	11-13-2001	Boyle	
		A6 *	6,403,312 B1	06-11-2002	Dahiyat et al.	
		A7 *	6,708,120 B1	03-16-2004	Mayo et al.	
		A8 *	2001/0032052 A1	10-18-2001	Mayo et al.	
		A9 *	2001/0039480 A1	11-08-2001	Mayo et al.	
	П	A10 *	2002/0004706 A1	01-10-2002	Mayo et al.	
		A11 *	2002/0009780 A1	01-24-2002	Dahiyat et al.	
	Γ	A12 *	2002/0048772 A1	04-25-2002	Dahiyat et al.	
		A13 *	2002/0090648 A1	07-11-2002	Dahiyat et al.	
	П	A14 *	2002/0106694 A1	08-08-2002	Mayo et al.	
		A15 *	2002/0110868 A1	08-15-2002	Dahiyat et al.	
		A16	2003/0013651 A1	01-16-2003	Lam et al.	
		A17 *	2003/0049654 A1	03-13-2003	Dahiyat et al.	·
		.A18 *	2003/0130827 A1	07-10-2003	Dahiyat et al.	
		A19 *	2003/0138401 A1	07-24-2003	Dahiyat et al.	
		A20 °	2003/0166559 A1	09-04-2003	Desjarlais et al.	
	T	A21 *	2003/0219864 A1	11-27-2003	Desjarlais et al.	
	$\overline{k}$	A22 *	2004/0043429 A1	03-04-2004	Dahiyat et al.	
DA	$\Pi$	A23 *	2004/0043430 A1	03-04-2004	Dahiyat et al.	

		-	F	OREIGN PATEN	T DOCUMENTS		
	miner	Cite No.	Foreign Patent Occument Country Code <sup>2</sup> Number <sup>4</sup> Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>4</sup>
P		B1 '	EP 0 974 111 B1	01-26-2000	California Institute of Technology		
		B2 '	WO 98/47089 A1	10-22-1998	California Institute of Technology		
	1	В3	WO 99/29865 A3	06-17-1999	The Rockefeller University		
2	1	B4 ·-	WO 00/15807 A1	03-23-2000	M & E Biotech		
XX	$/\vee$	B5 '	WO 00/23564 A2	04-27-2000	Xencor, Inc.		

Date Considered Examiner Signature

\*EXAMINER: Initial if reference considered, whether of not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

'Applicant's unique citation designation number (optional).

'See Kinds Codes of USPTO Patent Documents at <a href="https://www.uspto.gov">www.uspto.gov</a> or MPEP 901.04.

'Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.

16 if possible.

'Applicant is to place a check mark here if English Language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete. including gathering, preparing, and submitting the complete application form to the USPTO. Time will vary depending on the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

	Substitute for fo	nn 1449/	<b>√</b> PTO	Complete if Known					
	(Mod	lified)		Application Number	10/611,363				
IN	FORMATION	DISC	CLOSURE	Filing Date	July 1, 2003				
S.	TATEMENT E	BY AP	PLICANT	First Named Inventor	DESJARLAIS, John R.				
				Art Unit	1647				
	(use as many she	ets as ne	cessary)	Examiner Name	To Be Assigned K.M., XBM				
Sheet	2	of	6	Attorney Docket Number	A-71486-2				

Γ		FOREIGN PATENT DOCUMENTS												
ľ			niner als*	Cite No.	Foreign Patent Document Country Code <sup>2</sup> Number <sup>4</sup> Kind Code <sup>6</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T⁰					
t		A	M	B6 .	WO 01/59066 A2, A3	08-16-2001	Xencor, Inc.							
ľ		<b>+</b>	1	B7 *	WO 03/014325 A2, A3	02-20-2003	Xencor							
ľ	1	ń.		B8	WO 03/033663 A2	04-24-2003	Barnes-Jewish Hospital							
ľ	R	∜	7	B9	WO 03/033664 A2	04-24-2003	Barnes-Jewish Hospital							

			NON PATENT LITERATURE DOCUMENTS	
Exan Ipiti		Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the Item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T°
W.	IJ	C1	ADLER, S.H., and TURKA L.A., "Immunotherapy as a means to induce transplantation tolerance," Curr Opin Immunol, 2002 Oct, 14(5):660-5.	
	T	C2	ALATALO S.L., et al., "Rapid Screening Method for Osteoclast Differentiation in Vitro That Measures Tartrate-resistant Acid Phosphatase 5b Activity Secreted into the Culture Medium," Clin Chem, 2000 Nov, 46(11):1751-4.	
		СЗ	ANDERSON DM, et al., "A homologue of the TNF receptor and its ligand enhance T-cell growth and dendritic-cell function," Nature, 1997 Nov 13, 390(6656):175-9.	
		C4	ARRON JR, and CHO! Y, "Bone versus immune system," Nature, 2000 Nov 30, 408(6812):535-6.	
	T	C5	ATKINS GJ, et al., "Osteoprotegerin inhibits osteoclast formation and bone resorbing activity in giant cell tumors of bone," Bone, 2001 Apr, 28(4):370-7.	
	T	C6	BACHMANN MF, and KOPF M., "Balancing protective immunity and immunopathology," Curr Opin Immunol, 2002 Aug, 14(4):413-9.	
		<b>C7</b>	BIANCHI L, et al., "A cluster region of AP-1 responsive elements is required for transcriptional activity of mouse ODC gene by hepatocyte growth factor," Arch Biochem Biophys, 2002 May 1, 401(1):115-23.	
		СВ	BODMER JL, et al., "The molecular architecture of the TNF superfamily." Trends Biochem Sci., 2002 Jan, 27(1):19-26.	
		C9	CHILDS LM, et al., "In Vivo RANK Signaling Blockade Using the Receptor Activator of NF-kappaB:Fc Effectively Prevents and Ameliorates Wear Debris-Induced Osteolysis Via Osteodast Depletion Without Inhibiting Osteogenesis," J Bone Miner Res., 2002 Feb, 17(2):192-9.	
		C10	COLLIN-OSDOBY P, et al., "Receptor Activator of NF-kappa B and Osteoprotegerin Expression by Human Microvascular Endothelial Cells, Regulation by Inflammatory Cytokines, and Role in Human Osteoclastogenesis," J Biol Chem., 2001 Jun 8, 276(23):20659-72.	
		C11	COMPSTON JE., "Bone marrow and bone: a functional unit," J Endocrinol., 2002 Jun, 173(3):387-94.	
	$\int$	C12	CUROTTO de LAFAILLE MA, and LAFAILLE JJ., "CD4(+) regulatory T cells In autoimmunity and allergy," Curr Opin Immunol., 2002 Dec, 14(6):771-8.	
R		C13	DARNAY BG, et al., "Characterization of the intracellular domain of receptor activator of NF-kappaB (RANK). Interaction with tumor necrosis factor receptor-associated factors and activation of NF-kappab and c-Jun N-terminal kinase," J Biol Chem., 1998 Aug 7, 273(32):20551-5.	

	rí l				1	
Examiner Signature		21	Date Considered	9	510	16

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Applicant's unique citation designation number (optional). See Kinds Codes of USPTO Patent Documents at <a href="https://www.uspto.gov">www.uspto.gov</a> or MPEP 901.04. Senter Office that issued the document, by the two-letter code (WIPO Standard ST.3). For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. Applicant is to place a check mark here if English Language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the complete application form to the USPTO. Time will vary depending on the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Complete if Known Substitute for form 1449A/PTO (Modified) 10/611,363 Application Number INFORMATION DISCLOSURE Filing Date July 1, 2003 STATEMENT BY APPLICANT DESJARLAIS, John R. First Named Inventor Art Unit (use as many sheets as necessary) Examiner Name To Bo Assigned A-71486-2 6 Sheet Attorney Docket Number

L										
		NON PATENT LITERATURE DOCUMENTS								
Examine Initials	r Cite	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, di	7							
	C14	DEYAMA Y, et al., "Histamine stimulates production of osteoclast differentiation factor/receptor activator of nuclear factor- kappaB ligand by osteoblasts," Biochem Biophys Res Commun., 2002 Oct 25, 298(2):240-6.	$\prod$							
,	C15	FATA JE, et al., "The esteoclast differentiation factor esteoprotegerin-ligand is essential for mammary gland development," Cell., 2000 Sep 29,103(1):41-50.								
	C16	252(3):697-702.								
	C17	GOATER JJ, et al., "Efficacy of ex vivo OPG gene therapy in preventing wear debris induced osteolysis," J Orthop Res. 2002 Mar, 20(2):169-73.								
	C18	GOOD CR, et al., "Immunohistochemical study of receptor activator of nuclear factor kappa-B ligand (RANK-L) in human osteolytic bone tumors," J Surg Oncol., 2002 Mar, 79(3):174-9.								
	C19	GORI F, et al., "The expression of osteoprotegerin and RANK ligand and the support of osteoclast formation by stromal- osteoblast lineage cells is developmentally regulated," Endocrinology, 2000 Dec, 141(12):4768-76.	L							
	C20	GOWEN M et al., "Emerging theraples for osteoporosis," Exp. Opin. on Emerging Drugs, 2000, 5(1):1-43								
	C21	GRAVALLESE EM, et al., "The role of TNF-receptor family members and other TRAF-dependent receptors in bone resorption," Arthritis Res., 2001, 3(1):6-12.								
	C22	HOFBAUER LC, et al., "Interleukin-1beta and tumor necrosis factor-alpha, but not interleukin-6, stimulate osteoprotegerin ligand gene expression in human osteoblastic cells," Bone, 1999 Sep, 25(3):255-9.								
	C23	HOFBAUER LC, et al., "Receptor activator of nuclear factor-kappaB ligand and osteoprotegerin: potential implications for the pathogenesis and treatment of malignant bone diseases," Cancer, 2001 Aug 1, 92(3):460-70.								
	C24	HONORE P, et al., "Osteoprotegerin blocks bone cancer-induced skeletal destruction, skeletal pain and pain-related neurochemical reorganization of the spinal cord," Nat Med. 2000 May;6(5):521-8.								
	C25	HOTOKEZAKA H, et al., "U0126 and PD98059, specific inhibitors of MEK, accelerate differentiation of RAW264.7 cells into osteoclast-like cells," J Biol Chem., 2002 Dec 6, 277(49):47366-72.								
	C26	HSU H, et al., "Tumor necrosis factor receptor family member RANK mediates osteoclast differentiation and activation induced by osteoprotegerin ligand," Proc Natl Acad Sci U S A., 1999 Mar 30, 96(7):3540-5.								
	C27	HUBER DM, et al., "Androgens suppress osteoclast formation induced by RANKL and macrophage-colony stimulating factor," Endocrinology, 2001 Sep, 142(9):3800-8.	1							
	C28	IKEDA T, et al., "Determination of three isoforms of the receptor activator of nuclear factor-kappaB ligand and their differential expression in bone and thymus," Endocrinology, 2001 Apr, 142(4):1419-26.								
	C29	red 22, 277(8):6631-6.								
	C30	KANEDA T, et al., "Endogenous production of TGF-beta is essential for osteoclastogenesis induced by a combination of receptor activator of NF-kappa B ligand and macrophage-colony-stimulating factor," J Immunol., 2000 Oct 15, 165(8):4254-63.								
	C31	KITAZAWA R, and KITAZAWA S., "Vitamin D <sub>3</sub> augments osteoclastogenesis via vitamin D-responsive element of mouse RANKL gene promoter," Blochem Biophys Res Commun, 2002 Jan 18, 290(2):650-5.								
1	C32	KITAZAWA R, et al., "Promoter structure of mouse RANKL/TRANCE/OPGL/ODF gene," Biochim Biophys Acta., 1999 Apr 14, 1445(1):134-41.								
	C33	KONG YY, et al., "Activated T cells regulate bone loss and joint destruction in adjuvant arthritis through osteoprotegerin ligand," Nature, 1999 Nov 18, 402(6759):304-9.								

Signature

\*EXAMINER: Initial if reference considered, whether or not clation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

'Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at <a href="https://www.uspto.gov">www.uspto.gov</a> or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. Applicant is to place a check mark here if English Language Translation is attached.

Date Considered

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, Including gathering, preparing, and submitting the complete application form to the USPTO. Time will vary depending on the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Examiner

	Substitute for fo		A/PTO	Complete if Known .							
	(Modi	ified)		Application Number	10/611,363						
. IN	<b>IFORMATION</b>	DISC	CLOSURE	Filing Date	July 1, 2003						
S	TATEMENT B	Y AF	PLICANT	First Named Inventor	DESJARLAIS, John R.						
				Art Unit	1647						
	(use as many she	ets as ne	cessary)	Examiner Name	To Be Assigned L.M. PERM						
Sheet	4	of	6	Attorney Docket Number	A-71486-2						

Shee	et	4	of	6	/	Attorney Docket Nur	mber	A-71486-2		4			
				NON DAT		FERATURE DO	OCUM	ENTO	<del></del>	<u>_</u>			
										_			
Examiner Initiats	Citq No.							tem (book, magazine, journal, serial, symposium, ca country where published.		76			
W	<b>d</b> 34	LACEY DL, et al., 17, 93(2):165-76.		rotegerin ligand	is a cytoki	ine that regulates	osteoda	ast differentiation and activation," Cell,	1998 Apr				
	C35	RANK ligand," J C	Clin inves	st., 2000 Dec, 10	06(12):148	81-8. <sup>°</sup>		macrophages exposed to permissive le					
	C36	LAM J, et al., "Crys Invest., 2001 Oct,			NCE/RAN	IKL cytokine reve	als deter	erminants of receptor-ligand specificity,"	'J Clin				
$\prod$	C37			<u> </u>	•		•	n Pharmacol., 2002 Jun, 2(3):330-7.					
	C38	TRANCE," Bone, 2	LEAN JM, et al., "Osteoclast lineage commitment of bone marrow precursors through expression of membrane-bound TRANCE," Bone, 2000 Jul, 27(1):29-40.										
	C39	mass and calcium	I J, et al., "RANK is the intrinsic hematopoietic cell surface receptor that controls osteoclastogenesis and regulation of bone nass and calcium metabolism," Proc Natl Acad Sci U S A, 2000 Feb 15, 97(4):1566-71.										
	C40	94.						NF family ligands," Cell, 2002 Feb 8, 10		Ĺ			
	C41	104(4):487-501.			<u> </u>			mammalian biology," Cell, 2001 Feb 2		Ĺ			
	C42	LUM L, et al., "Evid of TRANCE, a TNI 274(19):13613-8.	IF family	r a role of a turn member involve	nor necrosi ed in osteo	is factor-alpha (The idastogenesis and	NF-alpha d dendri	a)-converting enzyme-like protease in s itic cell survival," J Biol Chem., 1999 Mi	shedding ay 7,				
	C43	and bone," Trends	s Endocri	rinol Metab., 200	01 Jan-Feb	b, 12(1):2-4.		B ligand (RANKL): another link between		Ĺ			
	C44	MATSUZAKI K, et mononuclear cell c	al., "Osf cultures,	teoclast different Biochem Biopl	tiation fact hys Res C	tor (ODF) induces commun., 1998 M	osteocl ay 8, 24	last-like cell formation in human periph 6(1):199-204.	eral blood	Ĺ			
	C45	McHUGH KP, et a 2000 Feb, 105(4):4			ntegrins are	e osteosclerotic b	ecause	of dysfunctional osteoclasts," J Clin In-	vest.,	Ĺ			
	C46	Clin Invest., 2000	Jun, 105	5(12):1833-8.	•			ne marrow cells in Paget's disease of b		Ĺ			
	C47	NAKAGAWA N, et Biochem Biophys I	t al., "RA Res Cor	NK is the essen	ıtial signali ac 18, 253	ing receptor for or (2):395-400.	steoclast	t differentiation factor in osteoclastoger	nesis,"	Ĺ			
	C48	NAKASHIMA T, et NF-kappaB ligand: 2000 Sep 7, 275(3	t: modula	ation of the expre	and functi ession by	ional difference of osteotropic factor	f membr s and cy	rane-bound and soluble receptor activa ytokines," Blochem Biophys Res Comm	itor of nun.,	Ĺ			
	C49	suppressing bone Mar 15, 61(6):2572	resorption 2-8.	ion and hypercal	ilcemia in a	a model of humora	al hyperc	uclear factor kappaB-igG Fc fusion pro calcemia of malignancy," Cancer Res.,	, 2001				
	C50	PENNINGER, Jose Conference, The H	ef, "Bon Hague, 7	es, Lymphocyte: The Netherlands	s, and Mar s, Sept. 22	mmalian Evolution -26, 2002 (Abstra	n," Socie ict).	ety for Biomolecular Screening 8th Annu	ual	Ĺ			
IDA	C51							rophage-colony stimulating factor is suf ct, 139(10):4424-7.	ficient for	Ĺ			
NUT	C52	QUINN JM, et ai.,	The ge	neration of high	ly enricher	d osteoclast-linea	ge cell p	populations," Bone, 2002 Jan, 30(1):16	4-70.	ĺ			

Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through clation if not in conformance and not considered. Include copy of this form with next communication to applicant.

'Applicant's unique citation designation number (optional).

'See Kinds Codes of USPTO Petent Documents at <a href="https://www.uspto.gov">www.uspto.gov</a> or MPEP 901.04.

'Enter Office that Issued the document, by the two-letter code (WIPO Standard ST.3).

'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.

16 if possible.

'Applicant is to place a check mark here if English Language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the complete application form to the USPTO. Time will vary depending on the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. Do NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450. Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

	Substitute for		A/PTO	Complete if Known							
	(Mo	dified)		Application Number	10/611,363						
II	NFORMATION	N DIS	CLOSURE	Filing Date	July 1, 2003						
S	STATEMENT I	BY AF	PPLICANT -	First Named Inventor	DESJARLAIS, John R.						
				Art Unit	1647						
	(use as many sh	eets as ne	cessary)	Examiner Name	Te Be Assigned						
Sheet	5	of	6	Attorney Docket Number	A-71486-2						

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the Item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	14
	C53	RODAN GA, and Martin TJ, "Therapeutic approaches to bone diseases," Science, 2000 Sep 1, 289(5484):1508-14.	
Ì	C54	ROMAS E, et al., "Involvement of receptor activator of NFkappaB ligand and tumor necrosis factor-alpha in bone destruction in meumatoid arthritis," Bone, 2002 Feb, 30(2):340-6.	
	C55	SABOKBAR A, et al., "Two distinct cellular mechanisms of osteodast formation and bone resorption in periprosthetic osteolysis," J Orthop Res., 2003 Jan, 21(1):73-80.	
	C56	SAIDENBERG KERMANAC'H N, et al., "Osteoprotegerin and inflammation," Eur Cytokine Netw., 2002 Apr-Jun, 13(2):144-53.	Ц
	C57	SCHLONDORFF J, et al., "Biochemical and pharmacological criteria define two shedding activities for TRANCE/OPGL that are distinct from the tumor necrosis factor alpha convertase," J Biol Chem., 2001 May 4, 276(18):14665-74.	
	C58	SCHOPPET M, et al., "RANK ligand and osteoprotegerin: paracrine regulators of bone metabolism and vascular function," Arterioscler Thromb Vasc Biol., 2002 Apr 1, 22(4):549-53.	
	C59	SENIOR K., "Vaccinating against bone destruction," Drug Discov Today, 2001 Dec 15, 6(24):1243-1244.	
	C60	SHEVDE NK, et al., "Estrogens suppress RANK ligand-induced osteoclast differentiation via a stromal cell independent mechanism involving c-Jun repression," Proc Natl Acad Sci U S A, 2000 Jul 5, 97(14):7829-34.	
	C61	SRIVASTAVA S, et al., "Estrogen decreases osteodast formation by down-regulating receptor activator of NF-kappa B ligand (RANKL)-induced JNK activation," J Biol Chem., 2001 Mar 23, 276(12):8836-40.	
	C62	SUDA T, et al., "Modulation of osteoclast differentiation and function by the new members of the tumor necrosis factor receptor and ligand families," Endocr Rev., 1999 Jun, 20(3):345-57.	
	C63	TAKAHASHI N, et al., "A new member of tumor necrosis factor ligand family, ODF/OPGL/TRANCE/RANKL, regulates osteoclast differentiation and function," Blochem Biophys Res Commun., 1999 Mar 24, 256(3):449-55.	
	C64	TAKAYANAGI H, et al., "RANKL maintains bone homeostasis through c-Fos-dependent induction of interferon-beta," Nature, 2002 Apr 18, 416(6882):744-9.	
	C65	TAKAYANAGI H, et al., "Signaling crosstalk between RANKL and interferons in osteoclast differentiation," Arthritis Res., 2002, 4(Suppl 3):S227-32.	
	C66	TEITELBAUM SL., "Bone resorption by osteoclasts," Science, 2000 Sep 1, 289(5484):1504-8.	
	C67	THEILL LE, et al., "RANK-L and RANK: T cells, bone loss, and mammalian evolution," Annu Rev Immunol., 2002, 20:795-823.	
	C68	TSUDA E, et al., "Isolation of a novel cytokine from human fibroblasts that specifically inhibits osteoclastogenesis," Biochem Blophys Res Commun., 1997 May 8, 234(1):137-42.	
	C69	UDAGAWA N, et al., "Origin of osteoclasts: mature monocytes and macrophages are capable of differentiating into osteoclasts under a suitable microenvironment prepared by bone marrow-derived stromal cells," Proc Natl Acad Sci U S A, 1990 Sep, 87(18):7260-4.	
	C70	VANDERKERKEN K, et al., "Recombinant osteoprotegerin decreases tumor burden and increases survival in a murine model of multiple myeloma," Cancer Res., 2003 Jan 15, 63(2):287-9.	
	C71	WEI S, et al., "Receptor activator of nuclear factor-kappa b ligand activates nuclear factor-kappa b in osteoclast precursors," Endocrinology, 2001 Mar, 142(3):1290-5.	
	C72	WEKERLE T, et al., "Mechanisms of transplant tolerance induction using costimulatory blockade," Curr Opin Immunol., 2002 Oct, 14(5):592-600.	

	10	 L	$\mathcal{L}$	<u> </u>			1	1_	
Examiner Signature		<u> </u>	M(	WA	Date Considered	$\mathcal{G}$	131	7	

\*EXAMINER: Initial if reference considered, whether or not bitation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Applicant's unique citation designation number (optional).

\*Applicant's unique citation designation number (optional).

\*\*For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. \*Kind of document by the appropriate symbols as Indicated on the document under WIPO Standard ST. 16 if possible.

\*\*Applicant is to place a check mark here if English Language Translation is attached.

This collection of Information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the complete application form to the USPTO. Time will vary depending on the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. Do NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450. Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

	Substitute for fo		VPTO	Complete if Known			
	(Mod	ified)		Application Number	10/611,363		
11	<b>IFORMATION</b>	DISC	CLOSURE	Filing Date	July 1, 2003		
S	STATEMENT BY APPLICANT			First Named Inventor	DESJARLAIS, John R.		
				Art Unit	1647 C A ()		
	(use as many she	ets as ne	cessary)	Examiner Name	To Be Assigned K. VV. Y. Y. X.		
Sheet	6	of	6	Attorney Docket Number	A-71486-2		

	$\equiv$			NON PATENT LITERATURE DOCUMENTS	
				HOIT MENT ENERGY DAGGETTE	_
	Exami Initia		Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	71
	W	J		WILLARD D, et al., "Expression, purification, and characterization of the human receptor activator of NF-kappaB ligand (RANKL) extracellular domain," Protein Expr Purif., 2000 Oct, 20(1):48-57.	
			C74	WONG BR, et al., "TRANCE is a novel ligand of the tumor necrosis factor receptor family that activates c-Jun N-terminal kinase in T cells," J Biol Chem., 1997 Oct 3, 272(40):25190-4.	
			C75	WUYTS W, et al., "Evaluation of the role of RANK and OPG genes in Paget's disease of bone," Bone, 2001 Jan, 28(1):104-7.	
	.0			YAMAGISHI T, et al., "Reciprocal control of expression of mRNAs for osteoclast differentiation factor and OPG in osteogenic stromal cells by genistein: evidence for the Involvement of topolsomerase II in osteoclastogenesis," Endocrinology, 2001 Aug, 142(8):3632-7.	
/	W	Ü	C77	YASUDA H,et al., "Osteoclast differentiation factor is a ligand for osteoprotegerin/osteoclastogenesis-inhibitory factor and is identical to TRANCE/RANKL," Proc Natl Acad Sci U S A, 1998 Mar 31, 95(7):3597-602.	

. 1/	1 100 100 1	<u> </u>		1 14	
Examiner Signature		2/X	Date Considered	1510	0

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. Applicant's unique citation designation number (optional). \*See Kinds Codes of USPTO Patent Documents at <a href="https://www.uspto.gov">www.uspto.gov</a> or MPEP 901.04. \*Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). \*For Japanese patent documents, the Indication of the year of the reign of the Emperor must precede the serial number of the patent document. \*Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. \*Applicant is to place a check mark here If English Language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the complete application form to the USPTO. Time will vary depending on the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450. Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Substitute PTO/SB/08A (07-05) Approved for use through 07/31/2008. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE ons are required to respond to a collection of information unless it contains a valid OMB control number.

Docket A-71486-2 (463077-240)

Under the Paperwork Reduction Act of 1995, no Substitute to them 1449A/RED

RMATION DISCLOSUR

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

	Complete if Known
Application Number	10/611,363
Filing Date	July 1, 2003
First Named Inventor	DESJARLAIS, John R.
Art Unit	1647
Examiner Name	TBA P.M. PARY

1						A
	Examiner Initials	Cite No. <sup>1</sup>	Document Number Number-Kind Code <sup>2</sup> (if knawn)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
Ī	NW N	A1 ††	US-2002-061525 A1	05-23-2002	Rodrigo et al.	
	TO T	A2 †	US-6242213 B1	06-05-2001	Anderson	

Attorney Docket Number

1

			FOREIGN PATENT	DOCUMENTS		
Examiner Initials*	Cite No.1	Foreign Patent Document Country Code <sup>2</sup> Number <sup>4</sup> Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	т•
	B1 †††	WO 00/15807 A *	03-23-2000	M & E Biotech		
	B2 ††	WO 00/67034 A	11-09-2000	Immunex Corporation		
	B3 †††	WO 01/25277 A	04-12-2001	Maxygen APS		
i	B4 †††	WO 01/42298 A	04-21-2001	Kombluth		
	B5 †††	WO 01/64889 A	09-07-2001	Xencor		
	B6 ††	WO 02/18445 A	03-07-2002	Biogen, Inc.		
	B7 ††	WO 02/36141 A	05-10-2002	Immunex Corporation		
	B8 ††	WO 03/006154 A	01-23-2003	Xencor, Inc.		
	B9 ††	WO 03/029420 A	04-10-2003	Genentech, Inc.		
	B10 ††	WO 03/059281 A	07-24-2003	Xencor		
	B11 ††	WO 2004/081043 A	09-23-2004	Xencor		
	B12 ††	WO 2004/089982 A	10-21-2001	Xencor		
NA	B13 ††	WO 2005/035570 A	04-21-2005	Xencor, Inc.		
	B14 ††	WO 99/12965 A	03-18-1999	Biogen, Inc.		

L					NON PATENT LITERATURE DOCUMENTS	
Examiner Cite No."		No."	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Τ <sup>6</sup>		
$ar{l}$	W.	$\mathcal{I}$	C1	ttt	Lacey D. L. et al. "Osteoprotegerin ligand is a cytokine that regulates osteoclast differentiation and activation" 'Cell Cell Press, Cambridge, NA, US, vol. 93, April 17, 1998, pps. 165-176 *	
			C2	†††	Steed, P.M. et al. "Inactivation of TNF signaling by rationally designed dominant-negative TNF variants" Science (American Assoc for the Advancement of Science) vol. 301, no. 5641, (2003) pps. 1895-1898	
			СЗ	†††	Yasuda H. Et. Al. "Osteoclast Differentiation factor is a ligand for osteoprotegerin/osteoclastogeneis –Inhibitory factor and is identical to TRANCE/RANKYL" <i>Proc. Of Natl. Acad of Sci.</i> , (1998) vol. 95, pps. 3597-3602 *	

4818-1235-2513\16/26/2006/10:32 AM		1 1 >	
Examiner Signature	NUM	Date Considered Q \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). 'See Kinds Codes of USPTO Patent Documents at <a href="https://www.uspto.gov">www.uspto.gov</a> or MPEP 901.04. 'Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 'For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 'Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. 'Applicant is to place a check mark here if English Language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the complete application form to the USPTO. Time will vary depending on the Individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: